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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/302,863	04/30/99	GOODWIN	R 2519

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EXAMINER	
ROMEO, D	
ART UNIT	**PAPER NUMBER**
1647	11

DATE MAILED: 11/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/302,863	Applic...(s) Goodwin et al.
	Examiner David Romeo	Group Art Unit 1647

☒ Responsive to communication(s) filed on *28 Aug 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *15-28* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *15-28* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6, 7*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1647.

2. Claims 15-28 are pending and being examined.

3. Applicant's election with traverse of group I, claims 1, 4, 7-10 in Paper No. 10 is acknowledged. The traversal is moot in view of examination of claims 15-28.

Specification

4. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The attempt to incorporate subject matter into this application at page 5, lines 28-30, by reference to WO 98/39361 and at page 6, lines 27-29, by reference to WO 98/18921, EP 0869180A1 and WO 98/27114 is improper because the definitions of TACI-L and TACI are necessary to describe the claimed invention and provide an enabling disclosure of the claimed invention. In any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a U.S. patent or application which itself incorporates "essential material" by reference, or (4) a foreign application. "Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112).

Claim Rejections - 35 USC § 112

5. Claims 15-28 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The definitions of TACI-L and TACI, critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The attempt to incorporate subject matter into this application at page 5, lines 28-30, by reference to WO 98/39361 and at page 6, lines 27-29, by reference to WO 98/18921, EP 0869180A1 and WO 98/27114 is improper because the definitions of TACI-L and TACI are necessary to describe the claimed invention and provide an

enabling disclosure of the claimed invention. In any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a U.S. patent or application which itself incorporates "essential material" by reference, or (4) a foreign application. "Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112).

6. Claims 15, 23, 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assaying for the level of binding of the TACI protein to the TACI-L protein, does not reasonably provide enablement for assaying for the level of interaction of the TACI protein and the TACI-L protein, wherein said assaying comprises assessing activation of TACI in a cell, wherein said assessing is measured by calcium influx. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. It is apparent from the claims and the specification that "assaying for the level of interaction" encompasses any and all cellular changes or effects which result from TACI/TACI-L interaction, including changes or effects which result from either TACI or TACI-L activation. See the specification at page 8, lines 5-9. Most chemical reactions and physiological activities

involve unpredictable factors. It is unknown whether TACI-L is a TACI agonist or antagonist and vice versa. Furthermore, the specification does not contain a working example of such cellular changes or effects which result from TACI/TACI-L interaction. The specification fails to provide guidance for, and working examples of, changes or effects that result from TACI-L activation. The skilled artisan is left to extensive, random, trial and error experimentation in order to determine the cellular changes or effects which result from TACI/TACI-L interaction. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

7. Claims 15-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for "TACI"; while being enabling for a polypeptide comprising the amino acid sequence of SEQ ID NO: 4, does not reasonably provide enablement for "TACI-L". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are directed to or encompass "TACI" and "TACI-L" proteins. The specification at page 5, lines 28-30, defines "TACI" by reference to WO 98/39361,

and at page 6, lines 27-29, defines "TACI-L" by reference to WO 98/18921, EP 0869180A1 and WO 98/27114. WO 98/39361 (page 19, lines 12-18) defines TACI as a receptor protein having the amino acid sequence of as shown in SEQ ID NO: 2 or allelic variants, homologs, and analogs thereof. There are no structural limitations to the allelic variants, homologs, and analogs. WO 98/18921 (page 34, lines 23-25) defines Neutrokine α (TACI-L) as including one or more amino acid substitutions, deletions or additions. There are no limitations on the number of amino acid substitutions, deletions or additions. The instant claims encompass any and all proteins that bind each other. The specification teaches a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 that binds a polypeptide comprising the amino acid sequence of SEQ ID NO: 4. However, the instant specification the instant specification does not identify those amino acid residues in the amino acid sequence of a TACI or a TACI-L which are essential for their biological activity and structural integrity and those residues which are either expendable or substitutable. In the absence of this information a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis before they could even begin to rationally design a functional TACI or TACI-L having other than a natural amino acid sequence. Furthermore, there are no working examples of such allelic, homologous, or analogous polypeptides. Moreover, there is a lack of predictability in the art. Predicting structure, hence function, from primary amino acid sequence data is extremely complex and there doesn't exist an efficient algorithm for predicting

the structure of a given protein from its amino acid sequence alone. See Bowie (u11)[1] page 1306, column 1, full paragraph 1, and Ngo (v11) page 433, full paragraph 1, and page 492, full paragraph 2. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

8. Claims 15-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to or encompass "TACI" and "TACI-L" proteins. The specification at page 5, lines 28-30, defines "TACI" by reference to WO 98/39361, and at page 6, lines 27-29, defines "TACI-L" by reference to WO 98/18921, EP 0869180A1 and WO 98/27114. WO 98/39361 (page 19, lines 12-18) defines TACI as a receptor protein having the amino acid sequence of as shown in SEQ ID NO: 2 or allelic variants, homologs, and analogs

[1]References cited by the examiner are in an alphanumeric format, such as "a1", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

thereof. There are no structural limitations to the allelic variants, homologs, and analogs. WO 98/18921 (page 34, lines 23-25) defines Neutrokine α (TACI-L) as including one or more amino acid substitutions, deletions or additions. The instant claims encompass any and all proteins that bind each other. The specification teaches a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 that binds a polypeptide comprising the amino acid sequence of SEQ ID NO: 4. These SEQ ID NOs: meet the written description and enablement provision of 35 U.S.C. 112, first paragraph. However, the claims are directed to or encompass sequences from other species, mutated sequences, allelic variants, splice variants, and sequences having some degree of identity similarity, or homology. None of these sequences meets the written description provision of 35 U.S.C. 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

With the exception of SEQ ID NOs: 2 and 4, the skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method

of isolation. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGFs were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NOs: 2 and 4 but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115).

9. The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim(s) 15-28 are indefinite because they recite the terms "TACI" and "TACI-L". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "TACI" and "TACI-L" an artisan cannot determine what additional limitations are placed upon a claim by the presence of these terms. The metes and bounds of the claim(s) are not clearly set forth.

There is a lack of antecedent basis for the limitations of claim 21. The metes and bounds of the claim(s) are not clearly set forth. It is suggested that the claims recite "wherein the

composition is formed by adding the test compound to a composition comprising the TACI protein and the TACI-L protein".

Claim 26 is rejected under 35 U.S.C. § 112, second paragraph, since it is a dependent claim that depends from itself, and makes no sense, since it is incomplete. In the interest of compact prosecution the claim will be interpreted as incorporating the limitations of the claim 25. This interpretation of the claim does not relieve applicant from the requirement to respond to the instant rejection.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 15, 19, 20, 23, 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chaudhary (6, cited by Applicants) in view of Bringman (a11).

Chaudhary teaches human TNRL1-α having an amino acid sequence that is identical to TACI-L, SEQ ID NO: 4, of the instant invention (page 117, line 10, through page 118, line 2; Figure 11A), soluble forms thereof (page 34, lines 14-32), and humanized antibodies thereto

(page 59, line 25). BJAB cells, a human B cell line, were treated with TNRL1-α and their survival was significantly reduced (page 118, lines 4-16). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention that BJAB cells express a receptor for TNRL1-α (paragraph bridging pages 32-33). There are no structural limitations to "TACI" recited in the instant claims. The BJAB cell receptor for TNRL1-α is a "TACI", absent evidence to the contrary. Treating BJAB cells with TNRL1-α and assaying for cell survival, as taught by Chaudhary, is a method comprising forming a composition comprising a TACI protein and a TACI-L protein and assaying for the level of interaction of the TACI protein and the TACI-L protein, wherein the interaction of TACI and TACI-L is identified. Chaudhary does not teach treating BJAB cells with TNRL1-α in the presence of a test compound, assaying for cell survival, wherein said compound affects the interaction of TACI and TACI-L.

Bringman teaches that the characterization and purification of lymphotoxin would be facilitated by antibody raised against the lymphotoxin active or receptor binding site or an adjacent region that neutralizes the cytotoxic activity of lymphotoxin (column 2, lines 22-26). A method is provided therein for obtaining lymphotoxin neutralizing antibody (paragraph bridging columns 7-8). Bringman does not teach treating BJAB cells with TNRL1-α in the presence of a test compound, assaying for cell survival, wherein said compound affects the interaction of TACI and TACI-L. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat BJAB cells with TNRL1-α and assaying for cell survival, as

taught by Chaudhary, and to make a neutralizing antibody, as taught by Bringman, against TNRL1-α and to test that antibody for neutralization of TNRL1-α bioactivity in the BJAB cell survival assay, with a reasonable expectation of success. Treating BJAB cells with TNRL1-α in the presence of an anti-TNRL1-α neutralizing antibody, and assaying for cell survival, wherein said antibody neutralizes the bioactivity of TNRL1-α identifies that antibody as a compound that affects the interaction of TACI and TACI-L. One of ordinary skill in the art would be motivated to make this modification because antibody raised against a TNRL1-α active or receptor binding site or an adjacent region that neutralizes the cytotoxic activity of TNRL1-α would facilitate characterization and purification of TNRL1-α. The invention is prima facie obvious over the prior art.

Conclusion

12. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Romeo whose telephone number is (703) 305-4050. The examiner can normally be reached on Monday through Friday from 6:45 a.m. to 3:15 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242.

Faxed draft or informal communications should be directed to the examiner at (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

David Romeo
Primary Examiner
November 18, 2000